

REMARKS

Claims 11-23, 25-27, 29 and 31-33 are pending in the application. Claims 14 and 15 have been amended. The amendments to the claims are fully supported by the specification.

In the October 5, 2007 Office Action, claims 11-16 and 21-23 were rejected under 35 U.S.C. § 102(e) as anticipated by McSwiggen et al. Claims 11-23, 25-27, 29 and 31-33 were rejected under 35 U.S.C. § 103(a) as being unpatentable over McSwiggen et al. in view of Holen et al. The specific grounds for rejection, and applicants' response thereto, are set forth in detail below.

Rejection under 35 U.S.C. §112 paragraph 2

Claims 14 and 15 have been amended to address the Examiner's contentions regarding lack of proper antecedent basis. More specifically, claim 14 has been amended to recite, in part, "said first stretch aligns." Claim 15 has been amended to recite, in part, "said first stretch is shifted." Accordingly, the rejection is moot and its withdrawal is respectfully requested.

Rejections Under 35 U.S.C. §103(a)

Claims 11-23, 25-27, 29 and 31-33 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over McSwiggen et al. in view of Holen et al. Specifically, the Examiner states:

It would have been obvious to one of ordinary skill in the art to incorporate mutations of dsRNA relative to a target gene, as taught by Holen et. al. in the dsRNA, as taught by McSwiggen et al.

Office Action at page 6. Applicants respectfully traverse. To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art (*see, In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974)). Applicants respectfully assert that the combination of McSwiggen and Holen fail to teach or suggest all the limitations of the claimed invention. In particular, McSwiggen does not teach at least a pattern of modified nucleotides and the combination with Holen fails to correct this insufficiency.

McSwiggen describes a chemistry-based nucleotide modification, i.e., a modification which is made depending on whether a nucleotide is a pyrimidine or a purine. For example, in Figs. 4 and 5, all the pyrimidine nucleotides are substituted. More specifically, and as

particularly noted by the examiner, in SEQ ID NO: 665 each and every pyrimidine is 2'-O-methyl modified. Accordingly, if one skilled in the art followed the methods described by McSwiggen, the resultant nucleotide sequence would not result in a discernible pattern but, rather, would produce a random sequence based entirely on the chance occurrence of a certain nucleotide base in the particular sequence. Applicants respectfully submit that the positioning of the individual modified nucleotides relative to the non-modified nucleotides, and more specifically, the positioning of modified nucleotides relative to the 5' and 3' ends of the individual strand/stretch forming the double-stranded structure is irrelevant according to McSwiggen. Accordingly, McSwiggen fails to teach or suggest a nucleic acid having the structure recited in the instant claims and withdrawal of the rejection respectfully is requested.

Further, applicants respectfully assert that the examiner erred by stating that the mere repetition of a 2'-position modified group forms a pattern. (page 5, lines 7-8). A repeating pattern of modified and non-modified groups implies that there is a smallest unit of a modified group and a non-modified group, and such smallest unit is repeated so that it is present at least twice:

[modified group - non-modified group]-[modified group - non-modified group]

Applicants respectfully assert that the examiner has failed to describe anything that one of ordinary skill in the art would recognize as a pattern. The occurrence of a pyrimidine or a purine in McSwiggen's sequences is happenstance and, indeed, the alleged "pattern" indicated in bold by the examiner in the Office Action has an irregular arrangement in terms of an irregular composition and length, respectively, of the modified and non-modified groups. Such randomly arranged nucleotides cannot be regarded as a pattern.

In contrast to the McSwiggen and Holen combination, according to the claimed invention, a nucleotide is modified to form a pattern depending on its position within the nucleotide sequence of a strand/stretch forming the double-stranded structure, i.e. positional or spatial modification. In this way, the relative positioning of such a nucleotide relative to a non-modified nucleotide and thus relative to the 5' and 3' ends, respectively, determines whether modification occurs. In other words, the modification seen along the individual strand/stretch is neither dependent on nor even driven by the chemical nature of the individual nucleotide along such strand/stretch, but rather, depends on the position of the individual nucleotide. Indeed, the

presence or absence of a particular nucleotide base, pyrimidine or purine, plays no role in determining whether a nucleotide is modified forming a pattern.

For at least the reasons expressed above, it is urged that the art references cited by the examiner, either singly or in combination, fail to teach, suggest or disclose all the limitations of the claims. Accordingly, a *prima facie* case of obviousness has not been established by the Examiner, and the rejection under 35 U.S.C. §103(a) should be withdrawn. Favorable action is solicited.

Rejections Under 35 U.S.C. §102

There are two outstanding novelty rejections. First, the examiner relies upon Crooke et al. as allegedly anticipating claims 11-16 and 21-23. In addition, the examiner cites McSwiggen as allegedly anticipating claims 11-16 and 21-23. Applicants respectfully traverse each of the rejections.

It is axiomatic that, for a prior art reference to be anticipatory, every element of the claimed invention must be identically shown in a single reference. In re Bond, 15 USPQ2d 1566 (Fed. Cir. 1990). Applicants traverse each anticipation rejection, since neither Crooke nor McSwiggen teaches every element of the rejected claims.

Crooke

Claims 11-16 and 21-23 stand rejected under 35 U.S.C. § 102(b) as anticipated by Crooke et al. Applicants traverse the anticipation rejection because Crooke does not teach each and every element of the rejected claims.

The examiner asserts that because “[e]ach group of 2'-methoxy modified nucleotides is repeated once” a pattern is formed. This “pattern” allegedly anticipates the present rejected claims. Applicants respectfully disagree. First, given the ordinary clear meaning of the term¹, the following arrangement to cannot be a pattern:

[2'-modification] – [ribonucleotide group] – [2'-modification]

The illustrated arrangement is the entirety of the disclosed sequence. There is no repetition of series, it is merely a single sequence. As discussed in the reply of July 12, 2006, applicants specification makes it clear that, within the context of the present invention, a

¹ The term “pattern” is recited once in Crooke to describe digestion in RNA:RNA duplexes and is unrelated to a pattern in the context of the rejection (Col. 49, ll. 10-14).

“pattern” is a regular arrangement of nucleotides. The nucleotide arrangements of Crooke fail to disclose such a pattern and accordingly, fail to disclose all the limitation of the claimed invention.

Second, even assuming *arguendo* that the examiner’s interpretation of the instant claims is correct (see pages 8-9 of the instant Office Action), Crooke fails to disclose the limitation of a pattern. The examiner states:

[s]econdly, the limitation of the flanking groups on one or both sides of a 2'-position modified group is interpreted to mean each 2'-position modified group in a pattern can be separated by one flanking group and the flanking group would therefore flank each 2'-position modified group on one side.

Accordingly, based on the examiner’s above quoted text, applicants’ invention comprises the following:

[[2'-modified group]-[flanking group]] - [[2'-modified group]-[flanking group]]

Each 2'-group/flanking group component is a repeating unit creating a pattern (“each 2'-position modified group in a **pattern**”)(emphasis added). Crooke merely has the single, non-repeating, arrangement listed above and thus, it fails to anticipate the claimed invention even under assumed conditions that are favorable to maintenance of the rejection.

Accordingly, because Crooke fails to teach, suggest or disclose each and every element of at least independent claim 11, it does not anticipate claim 11 and the claims dependent therefrom. Applicants therefore respectfully request withdrawal of the rejection under 35 U.S.C. §102(b).

McSwiggen

Claims 11-16 and 21-23 stand rejected under 35 U.S.C. § 102(e) as anticipated by McSwiggen et al. Applicants respectfully traverse.

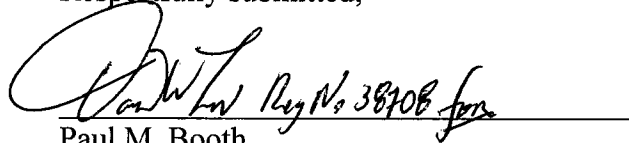
As described above, McSwiggen fails to teach each and every limitation of the claimed invention. More particularly, McSwiggen fails to teach a pattern. Accordingly, McSwiggen cannot anticipate the instant claimed invention and the rejection is moot. Favorable action is solicited.

CONCLUSION

In view of the foregoing amendments and remarks, applicants respectfully submit that the application is in condition for allowance. Should the Examiner feel that there are any issues outstanding after consideration of this response, the Examiner is invited to contact the undersigned to expedite prosecution of the application.

The Commissioner is hereby authorized by this paper to charge any fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-3840. **This paragraph is intended to be a CONSTRUCTIVE PETITION FOR EXTENSION OF TIME in accordance with 37 C.F.R. § 1.136(a)(3).**

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Paul M. Booth", is written over a horizontal line. To the right of the signature, the text "Reg. No. 38708" is handwritten.

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